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**Amendment and Response**

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Serial No.: 10/718,359

Confirmation No.: 3660

Filed: November 20, 2003

For: NACT AS A TARGET FOR LIFESPAN EXPANSION AND WEIGHT REDUCTION

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**Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1-11. (Cancel)

12. (Currently amended) An isolated polypeptide, wherein the polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:5 under stringent hybridization conditions, wherein the polypeptide is capable of Na<sup>+</sup>-dependent transmembrane transport of citrate, and wherein stringent hybridization conditions are 6X SSC, 5X Denhardt, 0.5% sodium dodecyl sulfate (SDS), and 100 µg/ml fragmented and denatured salmon sperm DNA hybridized overnight at 65°C and washed in 2X SSC, 0.1% SDS at least one time at room temperature for about 10 minutes followed by at least one wash at 65°C for about 15 minutes followed by at least one wash in 0.2X SSC, 0.1% SDS at room temperature for at least 3 to 5 minutes.

13. (Previously Presented) The isolated polypeptide of claim 12, wherein the polypeptide comprises SEQ ID NO:6.

14-19. (Cancel)

20. (Currently amended) An isolated polypeptide comprising an amino acid sequence having at least [[75%]] 95% identity to SEQ ID NO:6, wherein the polypeptide is capable of Na<sup>+</sup>-dependent transmembrane transport of citrate.

21. (Withdrawn) The isolated polypeptide of claim 20, wherein the encoded Na<sup>+</sup>-dependent transmembrane transport of citrate is modulated by Li<sup>+</sup>.

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22-26. (Cancel)

27. (Previously Presented) The isolated polypeptide of claim 20, wherein the polypeptide capable of Na<sup>+</sup>-dependent transmembrane transport of citrate requires multiple Na<sup>+</sup> ions for transport coupling.

28. (Previously Presented) The isolated polypeptide of claim 20, wherein the transmembrane transport of citrate is electrogenic.

29-49. (Cancel)

50. (Previously Presented) The isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 99% identity to SEQ ID NO:6.

51-56. (Cancel)

57. (Withdrawn/currently amended) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

- contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim [[12]] 20 with an agent;
- measuring citrate transport into the host cell in the presence of agent;
- and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;
- wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;
- wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

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58. (Withdrawn/currently amended) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim

[[12]] 20 with an agent;

measuring citrate transport into the host cell in the presence of agent;

and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;

wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;

wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

59. (Withdrawn/currently amended) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim

[[12]] 20 with an agent wherein the encoded Na<sup>+</sup>-dependent transmembrane transport of citrate is stimulated by Li<sup>+</sup>;

measuring citrate transport into the host cell in the presence of agent;

and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;

wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;

wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

60-75. (Cancel)

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76. (Withdrawn/currently amended) A method of identifying an agent that modifies Na<sup>+</sup>-dependent transmembrane citrate transporter activity comprising:

contacting a host cell expressing a Na<sup>+</sup>-dependent transmembrane citrate transporter of claim [[12]] 20 with an agent;

measuring the citrate-induced inward electrical current into the host cell in the presence of agent; and

comparing the citrate-induced inward electrical current into the host cell in the presence of the agent to the citrate-induced inward electrical current into the host cell in the absence of the agent;

wherein a decrease in the inward electrical current into the host cell in the presence of the agent indicates the agent is a blocker of Na<sup>+</sup>-dependent transmembrane citrate transporter activity;

wherein an increase in the inward electrical current into the host cell in the presence of the agent indicates the agent is a stimulator of Na<sup>+</sup>-dependent transmembrane citrate transporter activity.

77. (Withdrawn/currently amended) A method of identifying an agent that serves as a substrate of a Na<sup>+</sup>-dependent transmembrane citrate transporter comprising:

contacting a host cell expressing a Na<sup>+</sup>-dependent transmembrane citrate transporter of claim [[12]] 20 with an agent; and

determining the entry of the agent into the cell via the Na<sup>+</sup>-dependent transmembrane citrate transporter in the presence of agent;

wherein entry of the agent via the Na<sup>+</sup>-dependent transmembrane citrate transporter indicates the agent is a substrate of a Na<sup>+</sup>-dependent transmembrane citrate transporter.

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78. (Currently amended) A recombinant polypeptide, wherein the recombinant polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:5 under stringent hybridization conditions, wherein the recombinant polypeptide is capable of Na<sup>+</sup>-dependent transmembrane transport of citrate, and wherein stringent hybridization conditions are 6X SSC, 5X Denhardt, 0.5% sodium dodecyl sulfate (SDS), and 100 µg/ml fragmented and denatured salmon sperm DNA hybridized overnight at 65°C and washed in 2X SSC, 0.1% SDS at least one time at room temperature for about 10 minutes followed by at least one wash at 65°C for about 15 minutes followed by at least one wash in 0.2X SSC, 0.1% SDS at room temperature for at least 3 to 5 minutes.

79. (Previously Presented) The recombinant polypeptide of claim 78, wherein the recombinant polypeptide comprises SEQ ID NO:6.

80-81. (Cancel)

82. (Previously Presented) A recombinant polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO:6, wherein the polypeptide is capable of Na<sup>+</sup>-dependent transmembrane transport of citrate.

83. (Previously Presented) The recombinant polypeptide of claim 82, wherein the Na<sup>+</sup>-dependent transmembrane transport of citrate is modulated by Li<sup>+</sup>.